

**REMARKS**

Claims 25-29 are pending in the present case. The Examiner has rejected these Claims in an Office Action mailed June 2, 2004, and again in an Advisory Action mailed January 10, 2005, under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen TT et al. (J. Immunology 1994; 153:4775-4787) (hereinafter "Chen").

**1. Claims 25-29 recite the expression of at least three *different* variable regions.**

In the previously filed response, Applicant explained that Claims 25-29 recite the expression of at least 3 different variable regions (see, e.g., Claim 25, part b) using nucleic acid isolated from malignant B-cells. In the Advisory Action of January 10, 2005, the Examiner asserts that the claims do not require expression of three variable regions. Applicant respectfully disagrees. The claims expressly require expression of at least three different variable regions. In particular, the three different variable regions are recited to comprise any of the following combinations:

1. one V<sub>H</sub> region and at least two different V<sub>L</sub> regions (a total of three different variable regions)
2. two different V<sub>H</sub> regions and one V<sub>L</sub> region, (a total of three different variable regions.
3. two different V<sub>H</sub> regions and at least two different V<sub>L</sub> regions (a total of four different variable regions.

The claims indicate that the recited "at least two V<sub>L</sub> regions" are different V<sub>L</sub> regions by requiring that they differ from each other by at least one idiotope. Similarly, claims indicate that the recited "at least two V<sub>H</sub> regions" are different V<sub>H</sub> regions by requiring that they differ from each other by at least one idiotope. See, e.g., part (b) in each of Claims 25, 28 and 29.

Thus, the claims in the present application each require expression of at least 3 different variable regions to produce the claimed multivalent compositions.

**2. A single immunoglobulin does not provide at least three different variable**

**regions.**

Whole immunoglobulins (*e.g.*, such as those expressed by normal B-cells) comprise two identical heavy chains and two identical light chains (see, *e.g.*, the National Cancer Institute web page <http://press2.nci.nih.gov/sciencebehind/immune/immune10.htm>, a printed copy of which is attached hereto). A single immunoglobulin, therefore, provides only *two different* variable regions - one from the heavy chains and one from the light chains. Because the V<sub>H</sub> regions are identical to each other, the V<sub>H</sub> regions of a single immunoglobulin do not differ by any idiotopes. Similarly, the V<sub>L</sub> regions of a single immunoglobulin are identical to each other, and thus the V<sub>L</sub> regions do not differ by any idiotopes. For this reason, a single immunoglobulin provides only two different variable regions, *not the three different variable regions required by the present claims.*

**3. Chen provides only two different variable regions**

**A. Chen provides variable regions from a single immunoglobulin.**

As previously noted, the composition of Chen comprises variable regions of a single immunoglobulin, the 38C13 Id. See, *e.g.*, 4776, first sentence of column 1: "... we have shown that a fusion between *the* 38C13 tumor Id and GM CSF converts *the* tumor Id into a strong immunogen . . ." (*emphasis added*). Chen further makes clear that the antibody-cytokine fusion disclosed consists of heavy and light chain variable regions of only the 38C13 Id immunoglobulin, stating that "the resulting [chimeric Id] protein is composed of *the* 38C13 heavy chain variable region (V<sub>H</sub>38C) and *the* light chain variable region (V<sub>κ</sub>38C) fused to the human IgG1 heavy chain constant region (C<sub>γ</sub>1) and *κ* light chain constant region (C<sub>κ</sub>), respectively" (Chen, p4777, column 1, *emphasis added*).

**B. Chen does not disclose expression of at least three different variable regions.**

As noted above, a single immunoglobulin has only two different variable regions. Chen provides variable regions from only *a single immunoglobulin*. Specifically, Chen discloses one type of V<sub>H</sub> region, *i.e.*, the V<sub>H</sub>38C region (and thus does not provide at least two different V<sub>H</sub> regions). Similarly, Chen discloses only one type of V<sub>L</sub> region, V<sub>κ</sub>38C (and thus does not provide at least two different V<sub>L</sub> regions"). Chen thus discloses the

expression of only two different variable regions.

The fact that the V<sub>H</sub> and V<sub>L</sub> regions of Chen may differ from each other by one or more idiotopes is irrelevant to the present claims. As indicated in each of Claims 25, 28 and 29, the claimed compositions contain at least two V<sub>H</sub> regions that differ from each other by at least one idiotope, and/or at least two V<sub>L</sub> regions that differ from each other by at least one idiotope. A composition having idiotope differences only between V<sub>H</sub> and V<sub>L</sub> regions does not provide these claim elements.

**Claims 25-29 are not anticipated**

As previously noted, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The present claims recite the expression of at least **three different** variable regions of immunoglobulin molecules. Chen discloses a composition having only two different variable regions and fails to teach or suggest a composition comprising three different variable regions of immunoglobulins. More precisely, Chen does not teach or suggest any of combinations of variable regions expressly required by the claims:

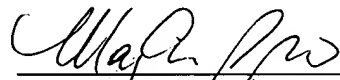
1. one V<sub>H</sub> region and at least two different V<sub>L</sub> regions (a total of three different variable regions)
2. two different V<sub>H</sub> regions and one V<sub>L</sub> region, (a total of three different variable regions.
3. two different V<sub>H</sub> regions and at least two different V<sub>L</sub> regions (a total of four different variable regions.

As such, the Chen reference does not teach each and every element as set forth in Claims 25-29, either expressly or inherently, and thus does not anticipate these claims under 35 U.S.C. § 102(b). Applicant thus respectfully requests that this rejection be removed.

**CONCLUSION**

For the reasons set forth above, it is respectfully submitted that all reasons for rejection should be removed and Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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